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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,056	03/31/2004	Maria Dalko	239466US0	4868
22850 7590 11/30/2007 OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER BLAND, LAYLA D	
			ART UNIT 1623	PAPER NUMBER
			NOTIFICATION DATE 11/30/2007	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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## Office Action Summary

Application No.

10/813,056

Applicant(s)

DALKO ET AL.

Examiner

Layla Bland

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 8, 12-15 and 17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-11, 16, 18-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This office action is a response to applicant's amendment submitted October 18, 2007, wherein claims 1-6 and 10 are amended and new claims 18-20 are added. This application claims priority to U.S. provisional application 60/471,725 filed May 20, 2003, and to French patent application 0304349 filed April 8, 2003. Claims 1-20 are pending in this application. Claims 8, 12-15, and 17 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-7, 9-11, 16, and 18-20 are examined on the merits herein.

The rejections of claims 1-5 under 35 USC 112, second paragraph, as being indefinite with regard to "X and Y form a ring of 6 or 7 carbon atoms..." are withdrawn in view of applicant's amendment.

The following rejection of record is maintained:

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the limitation "the compound according to claim 10." Claim 10 is drawn to a derivative, not a compound. There is insufficient antecedent basis for this limitation in the claim.

In the amendment submitted October 18, 2007, the scope of claims 1-7, 10, 11, 16 was changed and new claims 18-20 were added. The following new or modified rejections were necessitated by applicant's amendment submitted October 18, 2007:

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The three compounds for which the specification contains some data all have specific features in common:  $n=1$ , X and Y = NHMe, and  $R_1$  (or  $R_5$ ) = benzyl. A very large number of possible compounds exist which have not been reduced to practice and the specification gives no guidance on structure-function relationships.

See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee

will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed."

Claims 1-5 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds F, G, and K, (see Table 1, pages 15-18 of the specification) does not reasonably provide enablement for compounds wherein X and Y are other than NHMe, R<sub>5</sub> is other than benzyl, and n=0, or all compounds wherein m=1-3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApl's 1986) at 547 the court recited eight factors: (1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: the invention is a composition comprising compounds of formula (I).

The state of the prior art: Compounds of formula (I) are known in the art but have not been shown to be useful for topical application to the skin.

The relative skill of those in the art: The skill of those in the art is high.

The predictability or unpredictability of the art: Amides (X or Y = N), acids (X or Y = OH) and esters (X or Y = OR) have different chemical properties. Properties to be considered include acidity/basicity, hydrogen bonding, etc. For an example, see Son, et al. (J. Agric. Food Chem. 2002, 50, 468-472) wherein the free radical scavenging and antioxidative activity of caffeic acids, amides, and esters were compared [abstract and Table 1]. The number of hydroxy groups present ( $R_2$  = hydroxy or alkylhydroxy) also has a significant impact on the properties of a compound, including hydrophilicity/hydrophobicity, boiling point, and solubility. Consider, for example, glucose versus tetrahydropyran. Glucose has five hydroxy groups, is very soluble in water and has a melting point of around 146°C while tetrahydropyran has no hydroxy groups, is a liquid at room temperature and has a boiling point of 88°C [CRC Handbook of Chemistry and Physics].

The breadth of the claims: The claims allow for a number of substitutions at  $R_1$  as well as significant functional group substitutions at  $R_2$ , X and Y. m can be 0-4, and when m is 1-3, several isomers are possible.

The amount of direction or guidance presented: The specification presents several preferred embodiments of the compound but does not discuss the benefits or detriments of other claimed compounds. The specification does not present any guidance for isomers of compounds where  $m=1-3$ , other than compound G.

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The presence or absence of working examples: One example is given for the preparation of one of the claimed compounds. Batches of isolated stratum corneum were incubated in the presence of compounds F, G, and K and the freed corneocytes were counted by microscope. Compounds F, G, and K are structurally similar. In each case,  $n=1$ ,  $R_1$ =benzyl and X and Y = NHMe. No examples are given for the treatment of living skin.

The quantity of experimentation necessary: To practice the invention in keeping with the scope of these claims, a large number of compounds would have to be prepared. Considering the possible functional group substitutions at  $R_1$ , preparation of each of the claimed compounds could require extra synthetic steps besides those presented in the specification. For example, if  $R_1$  represents an alkyl group substituted with  $-COOR$  wherein  $R$  = ethyl, the ethyl ester could be hydrolyzed in the presence of sodium hydroxide during the final step of the synthesis in Figure 1 to give the acid instead of the target ester. The specification also does not give any guidance for the preparation of compounds wherein  $m=1-3$ , other than compound G. Several positional isomers are possible for such compounds, and the specification does not provide guidance or working examples for how to prepare these compounds. Once prepared, the compounds must be tested. No examples are presented regarding the testing of the claimed compounds on living skin.

Therefore, given the breadth of the claims, the lack of guidance and working examples, the unpredictability in the art, and the state of the art as discussed above,

undue experimentation would be required to make and use the claimed invention, and therefore, the invention is not enabled throughout the broad scope of the claims.

***Response to Arguments***

Applicant's arguments filed October 18, 2007 have been fully considered but they are not persuasive.

Applicant argues that the pending claims have been substantially narrowed and that the current scope of the claims satisfies the requirements under 35 USC 112, particular in view of the examples on pages 15-18.

Indeed, the scope of the claims has been narrowed. However, the scope of the claims has not been narrowed such that the claims represent what is described and enabled by the specification. As set forth above, working examples include only those compounds in which  $n=1$ ,  $R_1$ =benzyl and X and Y = NHMe, and of 12 compounds exemplified on pages 15-18, only one has X and Y=O. Furthermore, claims drawn to compounds wherein  $m=3$  have been added, and the specification provides no guidance as to how to prepare all the possible isomers of compounds wherein  $m=3$ . Thus, the rejection under 35 USC 112, first paragraph, still applies.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 1, the definition of  $R_2$  includes 0-4  $R_2$

groups but does not allow for them to independently defined. They are considered to be identical, which contradicts with many of the examples given in Table I of the specification.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2, as currently amended, ends with "C<sub>1</sub>-C<sub>12</sub> alkyl group,." The comma at the end of the claim implies that something else is intended to be included in the claim, but it is unclear what that is.

Claims 5-7, 9, and 16 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Claims 5-7, 9 and 16 are drawn to the composition of claim 1, wherein the compound of formula (I) is a C-glycoside derivative corresponding to formula (II), wherein S represents a monosaccharide. There is insufficient antecedent basis for this limitation in the claim. The definition of R<sub>2</sub> in claim 1, as amended, does not include -CH<sub>2</sub>OH. This substituent is necessarily present for the compound of formula (I) to be a C-glycoside derivative.

Claims 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Claims 18 and 19 each depend from claim 1 and each recite that R<sub>2</sub> can be hydroxymethyl. Hydroxymethyl is not included in the definition of R<sub>2</sub> provided in claim 1. There is insufficient antecedent basis for this limitation in the claims.

**Claim Rejections - 35 USC § 102**

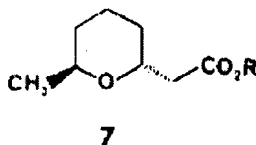
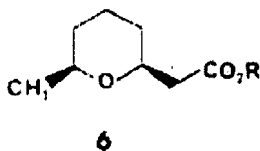
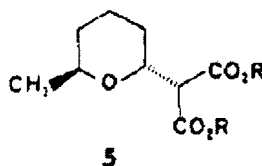
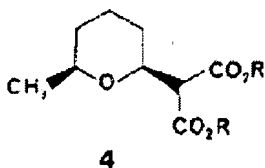
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Bates et al. (J. Org. Chem. 1983, 48, 4479-4481).

Bates et al teach the following compounds 4 and 5 [page 4480, Scheme 1]:



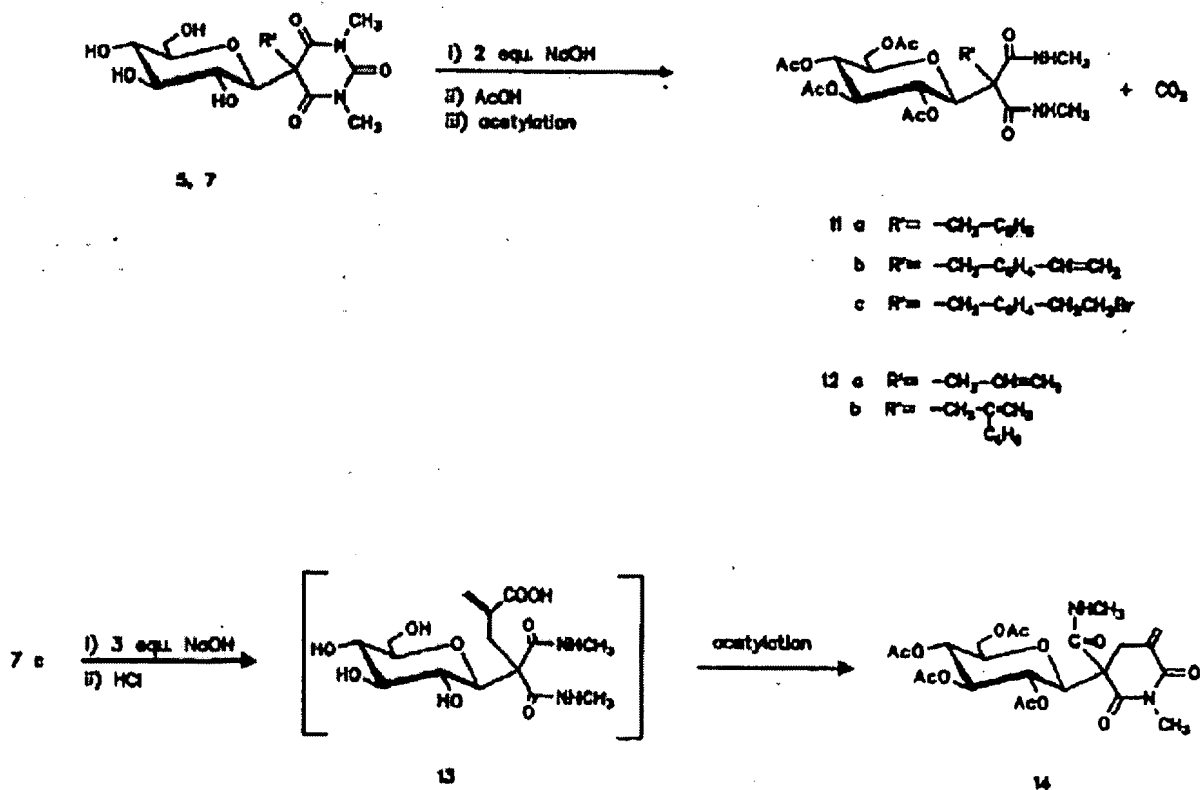
a, R = CH<sub>3</sub>  
b, R = H

In the case of compounds 4b and 5b, R<sub>1</sub> is hydrogen, R<sub>2</sub> is methyl, and X and Y are both OH. 4b and 5b were dissolved in a solution comprising water, a physiologically acceptable medium [page 4481, first and third paragraphs].

Claims 5-7, 9-11, 16, 18, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Wulff et al. (Carbohydrate Research 257 (1994) 81-95).

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Wulff et al. teach the following reaction [Scheme 3]:

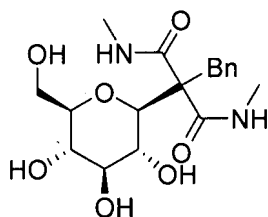


Scheme 3.

The products 11a-c are very similar to the claimed compounds, except that compounds 11a-c are acetylated and the claimed compounds are not. Wulff et al. teach that <sup>1</sup>H NMR spectra of their products were not informative due to the overlapping signals for the glycosyl ring and the allylic or benzylic CH<sub>2</sub>. Therefore, the products were characterized as the tetra-acetates [page 84, lines 4-7]. Experimental details for the production of the above compound 11a include that after hydrolysis of the starting material with sodium hydroxide the compound was acetylated [page 93, *Hydrolysis of barbiturate ring*]. The intermediate 13 clearly shows that the free hydroxy functions of

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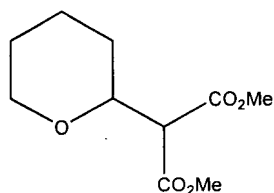
the compound are intact before acetylation. Therefore, the following compound with free hydroxy functions, which meets the limitations of claims 1, 3-7, 9-11, and 16, is necessarily present in the reaction before the acetylation step:



As applied to the instant claims, S represents a monosaccharide (glucose) comprising at least one free hydroxyl function and  $R_1$ =benzyl, X and Y are  $NHCH_3$ . According to the experimental details provided by Wulff, et al., the hydrolysis was carried out in water, which is a physiologically acceptable medium [page 93, lines 36-39].

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Kametani et al. (J. Am. Chem. Soc. 1987, 109, 3010-3017).

Kametani et al. teach compound 23 (shown below) [Table 1, Entry 1]. In this case,  $m=0$ ,  $R_1 = H$ , and X and Y are  $OCH_3$ . The compound is formed in acetone [Table 1, condition D]. Since acetone is used in nail polish remover, it is considered a “physiologically acceptable medium” that is compatible with the skin and the nails.



No claims are allowed in this application. The elected species of compound G appears to be free of the prior art.

### ***Response to Arguments***

Applicant's arguments filed October 18, 2007, regarding the prior art relied upon in the previous office action, have been fully considered but they are not persuasive.

Applicant argues that Wulff et al. and Kametani et al. no longer anticipate the compounds in claim 1 because they do not contain the required R<sub>1</sub> or R<sub>5</sub> group (Wulff et al.) or the required X or Y group (Kametani et al.).

In the compound taught by Wulff et al., the substituent corresponding to R<sub>1</sub> or R<sub>5</sub> is benzyl, which is encompassed by the definition of R<sub>1</sub> in claim 1 (alkyl group optionally substituted with aryl group) and R<sub>5</sub> in claim 10 (benzyl radical).

In the compound taught by Kametani et al., the substituents corresponding to X and Y are both -OMe, which is encompassed by the definition of X and Y in claim 1 (a radical -OR<sub>3</sub> wherein R<sub>3</sub> is a C1 alkyl group).

Applicant notes that claim 10 was not rejected over Kametani et al. Claim 10 is drawn to a C-glycoside derivative, which is not taught by Kametani et al. Thus, the claim was not rejected over Kametani et al.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Bland whose telephone number is (571) 272-9572. The examiner can normally be reached on M-R 8:00AM-5:00PM UST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Layla Bland  
Patent Examiner  
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November 21, 2007

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